Endothelial cells provide an instructive niche for the differentiation and functional polarization of M2-like macrophages.

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Public Summary:
It is now well recognized that the cells that give rise to blood are first generated from cells that line the inner part of blood vessels (called endothelial cells). Although this happens only during development, it is important to consider that we might be able to recapitulate these events in the petri dish upon adequate conditions. In this publication we present results that showed the ability of endothelial cells to support the growth of a specific subtype of blood cell (macrophages). Under our specific conditions, macrophages expand and differentiate when in contact with the endothelium. We further showed that these cells promote the formation of blood vessels and further contribute to the assembly of tubular structures from endothelial cells. The findings are important because for the first time it was demonstrated how to foster the expansion and specific differentiation of macrophages. The technology can be used to enhance neovascularization when necessary such as during wound healing.

Scientific Abstract:
Endothelial cells and macrophages are known to engage in tight and specific interactions that contribute to the modulation of vascular function. Here we show that adult endothelial cells provide critical signals for the selective growth and differentiation of macrophages from several hematopoietic progenitors. The process features the formation of well-organized colonies that exhibit progressive differentiation from the center to the periphery and toward an M2-like phenotype, characterized by enhanced expression of Tie2 and CD206/Mrc1. These colonies are long-lived depending on the contact with the endothelium; removal of the endothelial monolayer results in rapid colony dissolution. We further found that Csf1 produced by the endothelium is critical for the expansion of the macrophage colonies and that blockade of Csf1 receptor impairs colony growth. Functional analyses indicate that these macrophages are capable of accelerating angiogenesis, promoting tumor growth, and effectively engaging in tight associations with endothelial cells in vivo. These findings uncover a critical role of endothelial cells in the induction of macrophage differentiation and their ability to promote further polarization toward a proangiogenic phenotype. This work also highlights some of the molecules underlying the M2-like differentiation, a process that is relevant to the progression of both developmental and pathologic angiogenesis.